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Is Frozen-Section Diagnosis a Reliable Guide in Surgical Treatment of Stage I Endometrial Carcinoma?

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Acta Oncologica Vol. 41, No. 5, pp. 444–446, 2002

Frozen-section diagnoses and paraffin-section diagnoses were compared in 154 patients in stage I endometrial adenocarcinoma. In 134 (87%) of the 154 patients ($p < 0.001$), a corresponding depth of myometrial invasion was found, and in 132 (85.7%) patients the same tumor grade was established ($p < 0.001$). Frozen-section diagnosis of stage I endometrial adenocarcinoma is reliable for estimation of the extent of disease and accurately identifies patients who require surgical staging.

Received 6 November 2001
Accepted 18 March 2002

Endometrial carcinoma is the most common malignancy of the female genital tract in developed countries and is the fourth most common cancer in females. Although there is no accepted screening method, 75–80% of patients are diagnosed at early stage because of early symptoms such as bleeding disorders. Primary therapy for early stage endometrial carcinoma is surgery, and in FIGO stage I endometrial carcinoma, exact surgical staging is especially important in order to tailor adjuvant therapy.

The incidence of lymph node (LN) metastases in endometrial carcinoma increases with increasing tumor grade and depth of myometrial invasion (MI). Patients with grade 1 tumors involving only the endometrium and showing no evidence of intraperitoneal disease have almost no risk of nodal involvement. For patients with grade 2–3 tumors and depth of MI either less than 50% or more than 50%, the incidence of positive pelvic nodes is reported to be 5% and 34%, and that of positive para-aortic nodes 5% and 24% (1).

Boronow et al. studied 157 of 222 clinical stage I endometrial carcinoma patients who had undergone para-aortic LN sampling (2). The incidence of para-aortic LN metastases varied from 5% among patients with tumor confined to the endometrium or superficial myometrium to 38% in the group with deep MI. Similarly, Piver et al. found these rates to be 3% and 46%, respectively (3).

The aim of our study was to determine the accuracy of the frozen-section study in stage I endometrial adenocarcinoma, with reference to the paraffin-section diagnosis, in order to identify patients that do not require LN dissection. Although similar investigations have been published elsewhere (4–6), there is still some controversy concerning this matter.

MATERIAL AND METHODS

During the period from January 1995 to December 1999, 154 patients suffering from stage I endometrial adenocarcinoma and who had undergone surgery as the initial therapy were included in the study group. The endometrial cancer diagnosis was based on histology of endometrial curettage. The same team experienced in gynecologic oncology performed the operations. For all patients, intraoperative staging included peritoneal washing from the pelvis and abdomen, and a careful visual and palpatory exploration of the abdominal cavity. After completion of the total abdominal hysterectomy and bilateral salpingo-oophorectomy, the operative specimens were immediately investigated by the gynecopathologist. For evaluation of depth of MI, the uterus was opened and the cavity of the uterus was inspected for irregularities of contour and color. Three full-thickness slices were made through the wall of the uterus. The area of deepest macroscopic inva-

 ISSN 0284-186X

sion was selected for frozen-section diagnosis. If no tumor was apparent on gross examination, at least five random sections were performed. The prepared slides were then evaluated microscopically for extension of tumor invasion and tumor grade. The continuation of operation was based on frozen-section findings. The paraffin histologic slides were decisive in final evaluation of the depth of myometrial invasion and grade.

Surgical treatment consisted of total abdominal hysterectomy, bilateral salpingo-oophorectomy and washings for peritoneal cytology for tumors of no more than or less than 50% of myometrial invasion, and grade 1 tumors or grade 2 tumors smaller than 2 cm in diameter. For the remaining cases, pelvic and para-aortic LN dissections were performed. All patients were surgically staged according to the International Federation of Gynecology and Obstetrics guidelines (7).

The accuracy of the frozen section determining the depth of myometrial invasion and tumor grading was analyzed by kappa test. According to the test, less than 40% was inaccurate, 40–70% was moderately accurate and more than 70% was accurate.

RESULTS

The mean age of the patients was 56 ± 9 years (30–75 years) with a median of 56 years. According to paraffin-section evaluation, 21 patients (14%) had stage IA disease, whereas 101 patients (66%) had stage IB disease and 32 patients (21%) IC disease. One hundred and three patients (67%) had a grade 1 tumor, 36 (23%) had a grade 2 tumor and 15 patients (10%) had a grade 3 tumor.

Microscopic evaluation of the paraffin sections of the carcinomas agreed with frozen-section diagnosis for the depth of MI in 134 (87%) of the 154 patients. The 'measure of agreement Kappa' was found to be 0.742 for the depth of MI ($p < 0.001$) (Table 1). Paraffin-section diagnosis revealed that 132 (86%) of 154 patients had been diagnosed as having the same tumor grade by frozen-section diagnosis. The 'measure of agreement Kappa' was found to be 0.704 for the tumor grade ($p < 0.001$) (Table 2).

After analysis of the data, we found out that, according to the frozen-section diagnosis, we had over treated four patients and under treated two.

DISCUSSION

The goal of frozen-section diagnosis in endometrial cancer is to identify patients who are at high risk for pelvic and para-aortic lymph node metastases and who need surgical staging including pelvic/para-aortic lymphadenectomy.

Lagasse et al. reported a 1.6% incidence of intraoperative injuries and a 2.9% incidence of postoperative gastrointestinal and genitourinary complications in patients undergoing para-aortic lymphadenectomy (8). In the 1980s Belinson et al. considered para-aortic node dissection to be an investigational therapy, and they observed no serious complications resulting from para-aortic node dissection in 23 patients (9). Doering et al. also reported that no serious complications attributable to the procedure occurred among their 25 patients who had undergone para-aortic lymph node sampling because of estimated deep MI (4).

The risk from surgical therapy for endometrial cancer patients is primarily due to associated conditions such as obesity, diabetes, cardiovascular disease and other age-related factors. Outcome with respect to operating time, blood loss and complications is largely dependent on the weight and age of the patients and on the surgeon. The surgical staging patients have a 30–45 min longer operating time and a 60–150 ml greater blood loss than other patients. The reported rate of thromboembolic events in the larger series is 5% for the surgically staged patients, approximately twice the rate for patients who do not undergo pelvic and para-aortic node sampling (10, 11).

There is well-known correlation between tumor grade, myometrial invasion, and prognosis. The depth of MI and histologic grade has prognostic importance even in the absence of other adverse features. This is clearly demonstrated in a series of 390 surgically staged patients (12).

Table 1

Comparison of frozen-section diagnosis and final pathologic diagnosis, according to depth of myometrial invasion

		Paraffin section			
		No MI	< 1/2 MI	> 1/2 MI	Total
Frozen section	No MI	18	7	0	25
	< 1/2 MI	3	92	8	103
	> 1/2 MI	0	2	24	26
	Total	21	101	32	154

Abbreviation: MI = myometrial invasion.

Table 2

Comparison of frozen-section diagnosis and final pathologic diagnosis according to tumor grade

		Paraffin section			
		Grade 1	Grade 2	Grade 3	Total
Frozen section	Grade 1	96	7	1	104
	Grade 2	6	27	5	38
	Grade 3	1	2	9	12
	Total	103	36	15	154

Only 3.8% of patients with grade 1 tumors and less than a middle-third of MI suffered a relapse compared with 19% of patients with grade 3 cancers and a middle to outer one-third invasion.

Doering et al. reported that intraoperative gross visual examination of the cut surface of the tumor accurately determined the depth of MI in stage I endometrial adenocarcinoma with 71% sensitivity, 96% specificity and 80% positive predictive value (4). They also reported that intraoperative assessment of the depth of MI is a simple, inexpensive and useful technique for selecting those patients with stage I endometrial adenocarcinoma who might benefit from selective para-aortic lymphadenectomy.

Kucera et al. evaluated the accuracy rate of frozen-section diagnosis in their 70 patients suffering from stage I endometrial adenocarcinoma (5). They found the overall accuracy rate of frozen-section diagnosis in their 70 patients for depth of MI and tumor grade to be 80 and 84%, respectively. When five comparable studies were combined 624 patients, the accuracy rate of frozen-section diagnosis for MI and tumor grade was 88 and 84%, respectively. Using a minimum of four transverse cuts through the tumor and the entire thickness of the myometrium, Fanning & Firestein reported an accuracy of 95% for MI in frozen-section diagnosis (13), while Noumoff et al. reported an accuracy of 72% with one or two sections (6). Whereas in the majority of the previous studies one to four sections were made, we used a minimum of three sections through the entire thickness of the uterine wall.

Because endometrial cancer patients are frequently elderly and obese, and may have multiple underlying medical problems such as hypertension and diabetes mellitus, they are likely to be poor candidates for extended surgical procedures. However, identification of patients with para-aortic nodal metastases may permit appropriately individualized therapy, thus improving survival. Frozen-section diagnosis for endometrial adenocarcinoma stage I is a reliable guide in estimation of the extent of disease and accurately identifies patients who require surgical staging, making it an important tool for optimal, individualized treatment.

REFERENCES

1. Takeshima N, Hirai Y, Tanaka N, Yamawaki T, Yamauchi K, Hasumi K. Pelvic lymph node metastases in endometrial cancer with no myometrial invasion. Obstet Gynecol 1996; 88: 280–2.
2. Boronow RC, Morrow CP, Creasman WT, et al. Surgical staging in endometrial cancer: clinical-pathologic findings of a prospective study. Obstet Gynecol 1984; 63: 825–32.
3. Piver MS, Lele SB, Barlow JJ, Blumenson L. Paraaortic lymph node evaluation in stage I endometrial carcinoma. Obstet Gynecol 1982; 59: 97–100.
4. Doering DL, Barnhill DR, Weiser EB, Burke TW, Woodward JE, Park RC. Intraoperative evaluation of depth of myometrial invasion in stage I endometrial adenocarcinoma. Obstet Gynecol 1989; 74: 930–3.
5. Kucera E, Kainz CH, Reinthaller A, et al. Accuracy of intraoperative frozen-section diagnosis in stage I endometrial adenocarcinoma. Gynecol Obstet Invest 200; 49: 62–6.
6. Noumoff JS, Menzin A, Mikuta J, Lusk EJ, Morgan M, LiVolsi VA. The ability to evaluate prognostic variables on frozen section in hysterectomies performed for endometrial carcinoma. Gynecol Oncol 1991; 42: 202–8.
7. International Federation of Gynecology and Obstetrics. Corpus cancer staging. Int J Gynecol Obstet 1989; 28: 190.
8. Lagasse LD, Creasman WT, Shingleton HM, Ford JH, Blessing JA. Results and complication of operative staging in cervical cancer: experience of the Gynecologic Oncology Group. Gynecol Oncol 1980; 9: 90–8.
9. Belinson JL, Spirou B, Mc Clure M, Badger G, Pretorius RG, Roland TA. Stage I carcinoma of the endometrium: a 5-year experience utilizing preoperative cesium. Gynecol Oncol 1985; 20: 325–35.
10. Larson DM, Johnson K, Olson KA. Pelvic and paraaortic lymphadenectomy for surgical staging of endometrial cancer: morbidity and mortality. Obstet Gynecol 1992; 79: 998–1001.
11. Moore DH, Fowler Jr WC, Walton LA, Droegemueller W. Morbidity of lymph node sampling in cancers of the uterine corpus and cervix. Obstet Gynecol 1989; 74: 180–4.
12. Morrow CP, Bundy BN, Kurman RJ, et al. Relationship between surgical pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. Gynecol Oncol 1991; 40: 55–65.
13. Fanning J, Firestein S. Prospective evaluation of the morbidity of complete lymphadenectomy in endometrial cancer. Int J Gynecol Cancer 1998; 8: 270–3.